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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/579,263	07/01/2008	Alfred Werner Widmer	990784.00004	6586
26735	7590	07/29/2010		
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EXAMINER				
ROBINSON, BINTA M				
ART UNIT		PAPER NUMBER		
1625				
NOTIFICATION DATE		DELIVERY MODE		
07/29/2010		ELECTRONIC		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

pat-dept@quarles.com

### Office Action Summary

**Application No.**

10/579,263

**Applicant(s)**

WIDMER ET AL.

**Examiner**

BINTA M. ROBINSON

**Art Unit**

1625

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on Applicant remarks filed 4/19/2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) 9-17 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-8 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB-08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

**Detailed Action**

The 102 (b) rejection over Salvino is withdrawn and rendered moot in light of applicant's remarks and amendments. The 102 (b) rejection over Tamaki et. al. is withdrawn and rendered moot in light of applicant's remarks. The 102 (b) rejection of claims 1, 2, 6, and 7 over Vial et. al., is rendered moot because of applicant's remarks, with the exception that the examiner differs with the applicant's reasoning as to why the Vial et. al. reference is overcome because -R3 and R6 equal  $-\text{CH}_2\text{CH}_2=$  not  $-\text{CH}_2\text{CH}_2\text{C}=\text{CH}$  as the applicant claims. The 102 (b) rejection over Kocharyan et. al. is rendered moot in light of applicant's remarks. The 112, second paragraph rejection of claims 1-8 is rendered moot in light of applicant's amendment to the claims. Claims 11-17 are withdrawn from examination as being drawn to a non-elected invention.

1. **(new rejection)**

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. The phrase "A bis-cationic compound wherein the bis-cation of the compound is of Formula (I)" in line 1 and everywhere else throughout claims 1-8, as well as the deletion of the phrase "and salts thereof;" in line 6, page 5 of claim 1 and everywhere else throughout the claims – render these claims indefinite because it is not clear if the compound only consists of the bi-cation and no anion – and because it is known to one

of ordinary skill in the art that neither anions or cations can not exist in isolation, as the total electrical charge must be in balance. Since ions of like charge repel each other, they do not usually exist on their own. Instead, many of them may form a crystal lattice, in which ions of opposite charge are bound to each other. The applicant is claiming a compound as a cation. However, it is well known to one of ordinary skill in the art that **Quaternary ammonium salts or quaternary ammonium compounds** are salts of quaternary ammonium cations with an anion.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making and using salts of the bis-cationic compounds of formula I, does not reasonably provide enablement for making and using the bis-cationic compounds of formula I that do not contain anions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. It is known to one of ordinary skill in the art that neither anions or cations usually can exist in isolation, as the total electrical charge must be in balance. Since ions of like charge repel each other, they do not usually exist on their own. Instead, many of them may form a crystal lattice, in which ions of opposite charge are bound to each other. Yet, the applicant is claiming a compound as a cation.

There are many factors to be considered when determining whether there

is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art 6) the amount of direction provided by the inventor 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In *re Wands*, 858 F. 2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

a) Determining if any particular claimed compounds of formula I with no anions, would be active, would require synthesis of these cations and subjecting them to testing with Applicants' in vitro antibacterial assay and in vitro antifungal activity assay, haemolytic activity assay, pancreatic phospholipase assay, and antifungal susceptibility testing. Considering the large number of cations to be made, this is a large quantity of experimentation. b) The direction concerning the claimed compounds is found at pages 51-71. c) In the instant case, none of the working examples consist of only cations of formula I tested in applicant's assays.

6. d) The nature of the invention is inhibition of phospholipase and treatment of diseases with Applicants' compounds. This involves physiological activity. The nature of the invention requires an understanding of phospholipases A, B, C, and D, the binding activity of small ligands to phospholipases, and the ability of those

compounds to inhibit phospholipases. In view of the unpredictability of binding activity and the claimed divergent compounds and their cations, the skilled artisan would indeed question the inclusion cations as compounds since ions of like charge repel each other, they do not usually exist on their own. Instead, many of them may form a crystal lattice, in which ions of opposite charge are bound to each other. Yet, the applicant is claiming a compound as a cation.

7. e) There is no reasonable basis for the assumption that the myriad of compounds embraced the by present formula (I) will all share the same biological properties salts of these compounds. It is known to one of ordinary skill in the art that neither anions or cations usually exist in isolation, as the total electrical charge must be in balance. Since ions of like charge repel each other, they do not usually exist on their own. Instead, many of them may form a crystal lattice, in which ions of opposite charge are bound to each other.

The cations and their salts are chemically non-equivalent and there is no basis in the prior art for assuming in the non-predictable art of pharmacology that structurally dissimilar compounds will have such activity, *In re Surrey* 151 USPQ 724 (compounds actually tested which demonstrated the asserted psychomotor stimulatory and anti-convulsant properties were those having the 3,4-dichlorophenyl substituent at the 2-position on the thiazolidone nucleus not sufficient for enablement of any heterocyclic radical at the same position). *In re*

*Fouche*, 169 USPQ 429 at 434 (a Markush group including both aliphatic and heterocyclic members not enabled for the use of those compounds within the claim having heterocyclic moieties.) *In re CAVALLITO AND GRAY*, 127 USPQ 202 (claims covering several hundred thousand possible compounds, of which only thirty are specifically identified in appellants' application, not enabled unless all of the thirty specific compounds disclosed had equal hypotensive potency because that fact would strongly indicate that the potency was derived solely from the basic structural formula common to all of them. A wide variation in such potency would suggest that it was due in part to the added substituents and might be eliminated or even reversed by many of the possible substituents which had not been tried.)

f) The artisan using Applicants' invention to treat diseases with the claimed compounds would be a physician with a MD degree or a medicinal chemist with a PhD and several years of experience. She/He would be unaware of how to predict *a priori* how a changing a salt of the compound of formula I to its cationic form would affect biological activity. The skilled artisan would indeed question the claiming of the compounds as cations and the disclaiming of salts containing both the cation of formula I and an anion. g) Physiological activity, is well-known to be unpredictable, *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and

physiological activity). See also *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *In re Vaeck*, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). h) The breadth of the claims includes all of thousands of compounds of formula (I). Thus, the scope is very broad.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Binta M. Robinson whose telephone number is (571) 272-0692. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0670.

A facsimile center has been established. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machine are (703)308-4242, (703)305-3592, and (703)305-3014.



Art Unit: 1625

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-1600.

/Binta M Robinson/  
Examiner, Art Unit 1625

/Janet L. Andres/  
Supervisory Patent Examiner, Art Unit 1625